

In the Claims

Please cancel claims 40-42 without prejudice.

Please add the following new claims:

Sub B
~~19~~ 46. (New) The method of Claim ~~15~~, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (NSAID).

~~22~~ 46. (New) The method of Claim ~~19~~, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (NSAID).

~~28~~ 47. (New) The method of Claim ~~26~~, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (NSAID).

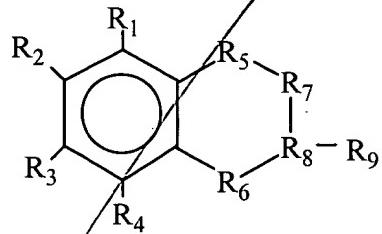
~~34~~ 48. (New) The method of Claim ~~27~~, wherein the antiinflammatory compound is a nonsteroidal, antiinflammatory drug (NSAID).

Please amend Claims 7-12, 16, 18-20, 22, 24-28 and 44 as follows:

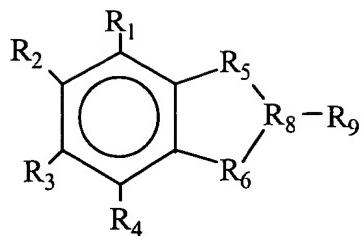
B3
~~17~~ 1. (Twice amended) An angiogenesis inhibitory composition comprising an angiogenesis inhibiting compound and an anti-inflammatory drug, wherein the angiogenesis inhibiting compound is selected from:

(1) a compound selected from the formula

A)

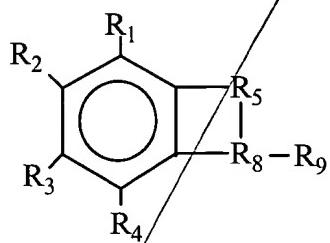


B)



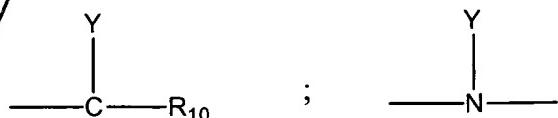
or

C)

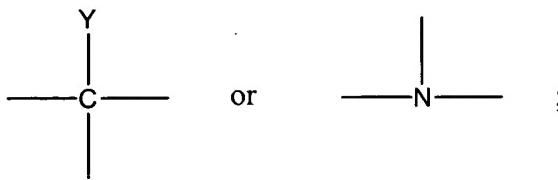


wherein

R₁ - R₄ are each independently selected from -H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; -XO_n or -O-XO_n, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens; R₅ - R₇ are each independently selected from

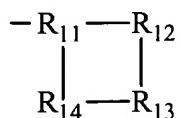


or -O-, where Y is absent and R₁₀ is =O or Y and R₁₀ are each independently the same as R₁; where R₈ is independently selected from:

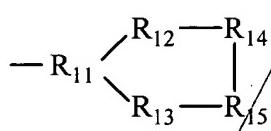


and R_9 is a moiety selected from

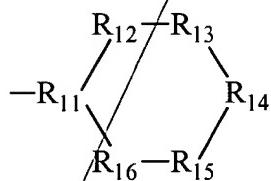
D)



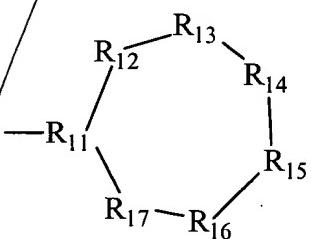
E)



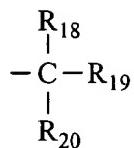
F)



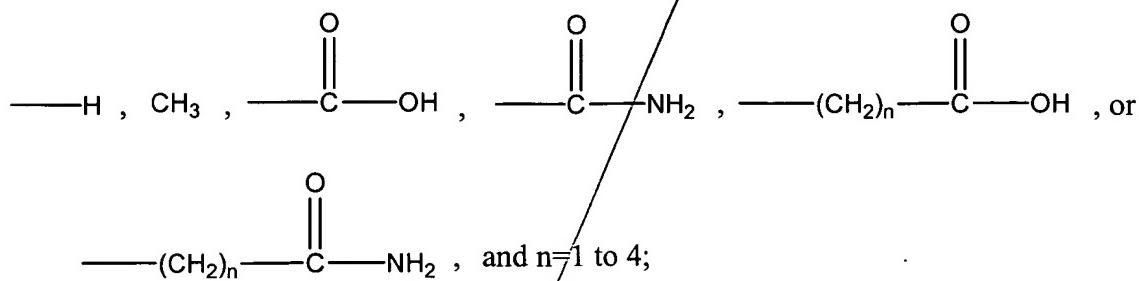
G)



or H)

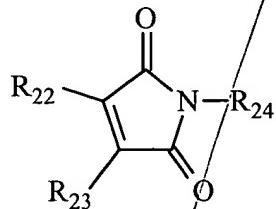


wherein each of R₁₂- R₁₇ is independently the same as R₅, wherein R₁₁ is independently the same as R₈; and wherein R₁₈, R₁₉ and R₂₀ are each independently selected from



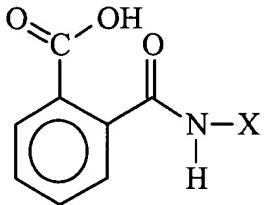
with the proviso that the angiogenesis inhibiting compound is not thalidomide;
(X) Song

(2) a compound selected from the formula

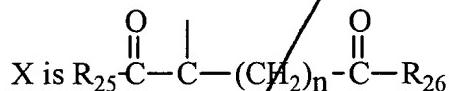


where R₂₂ and R₂₃ are each independently H, F, Cl, Br, I, CH₃, or -CH₂-CH₃; and R₂₄ is H, CH₃, or -CH₂-CH₃;
and

(3) a compound selected from the formula



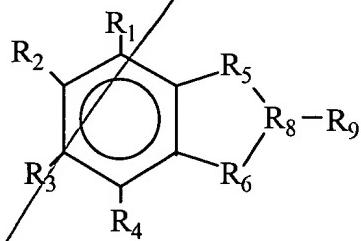
where X is R₆ as defined in (1) above, or



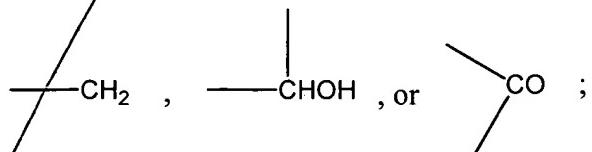
and R₂₅ and R₂₆ are independently -OH, -H, or -NH₂, and n = 1 through 4.

~~28.~~ (Amended) The angiogenesis inhibitory composition of Claim ~~1~~
wherein the angiogenesis inhibiting compound has the formula

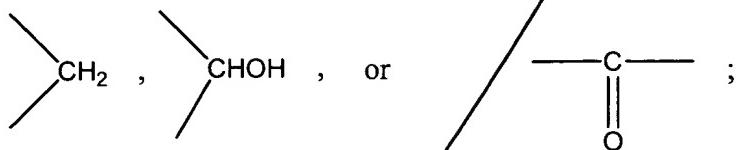
B)



wherein R₁-R₄ are as defined in Claim 7; R₅ and R₆ are independently selected from



and R₉ is selected from F) or H) wherein R₁₄ and R₁₆ are each independently selected from

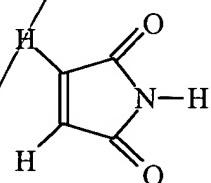


and R₁₅ is -O- or $\overset{R_{21}}{\underset{|}{\text{N}}}$, where R₂₁ is H, CH₃, or OH.

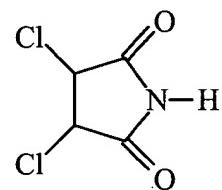
~~3~~ (Amended) The angiogenesis inhibitory composition of claim ~~7~~¹
wherein the angiogenesis inhibiting compound is selected from

B4
cont

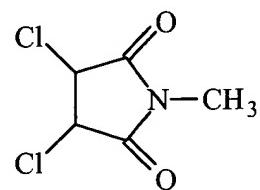
I)



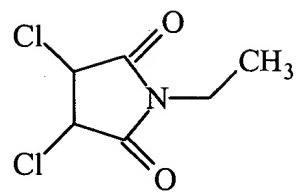
J)



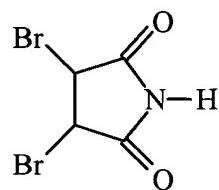
K)



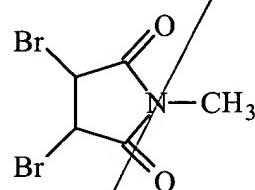
L)



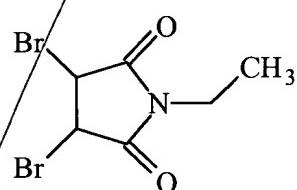
M)



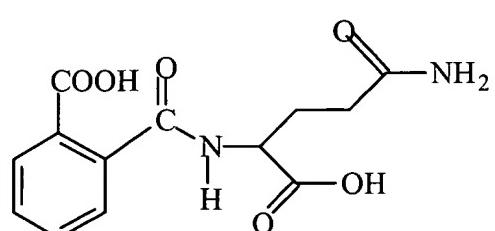
N)



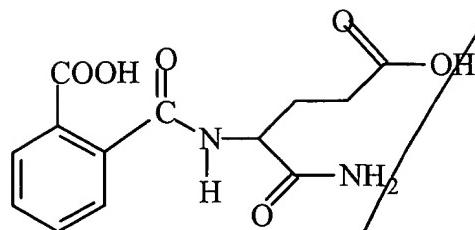
O)



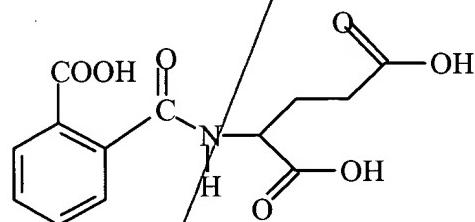
P)



Q)

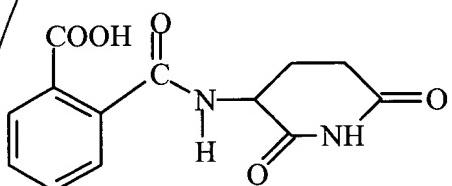


R)



or

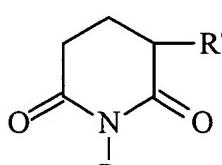
S)



~~10.~~ (Amended) The angiogenesis inhibitory composition of Claim ~~10~~,
wherein the angiogenesis inhibiting compound is selected from metabolites of
thalidomide, thalidomide analogs, epoxides of thalidomide, hydrolysis products thereof,
hydrolysis products of thalidomide, EM-12, metabolites of EM-12, epoxides of EM-12,
hydrolysis products thereof, EM-138, metabolites of EM-138, epoxides of EM-138,
hydrolysis products thereof, N-phthaloyl-DL-glutamic acid (PGA), N-phthaloyl-DL-
glutamine anhydride, or mixture thereof.

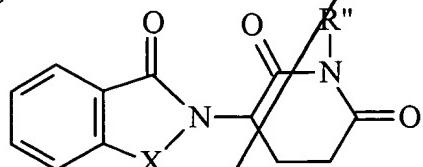
5 11. (Amended) The angiogenesis inhibitory composition of Claim 10
wherein the angiogenesis inhibiting compound is selected from

(I)



or

(II)



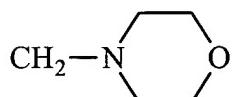
E1
B4
Cont

wherein

R is selected from H, (C₁-C₆)alkyl, phenyl, or benzyl; and R' is selected from phthalimido or succinimido;

wherein

X is CH₂ or C=O; and R'' is H, -CH₂CH₃, -C₆H₅, -CH₂C₆H₅, -CH₂CH=CH₂, or



or (III) hydrolysis products of (II)

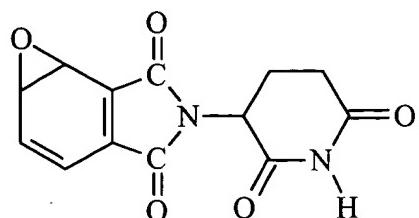
wherein

R'' is H and the piperidino ring or both the piperidino and the imido ring are hydrolyzed.

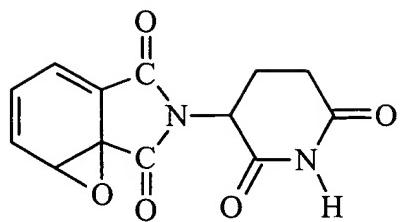
8 12.

(Amended) The angiogenesis inhibitory composition of Claim 10
wherein the angiogenesis inhibiting compound is selected from

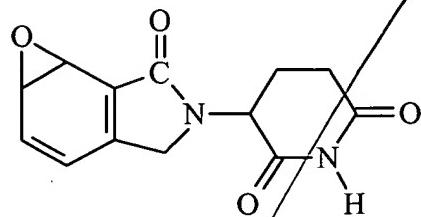
III



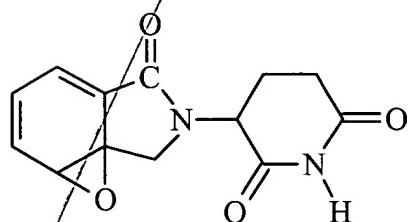
IV)



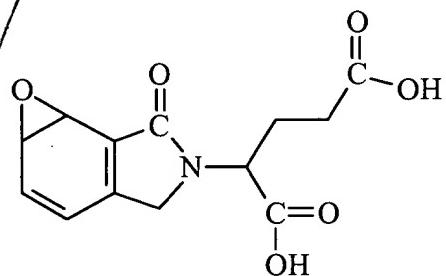
V)



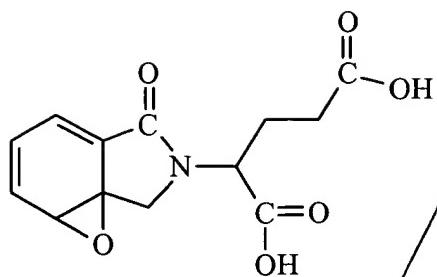
VI)



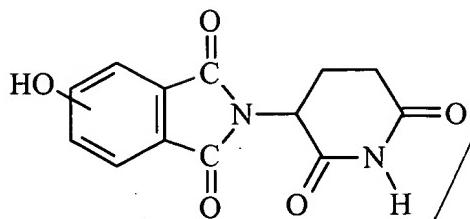
VII)



VIII)

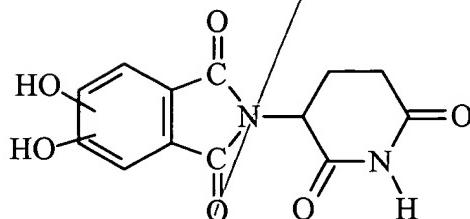


IX)

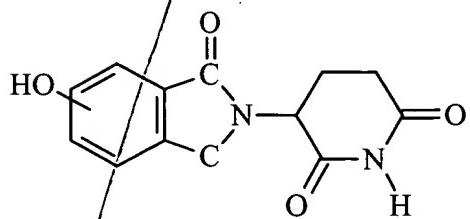


~~Ex~~
~~By~~
Cont

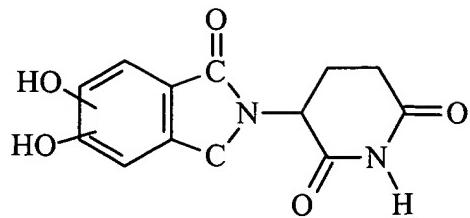
X)



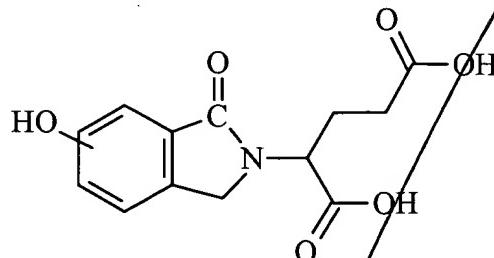
XI)



XII)



XIII)

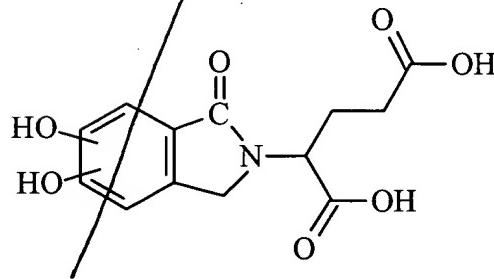


or

El

B7
cont

XIV)



BS

16. (Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal a composition comprising a nonsteroidal, anti-inflammatory drug (NSAID) with the proviso that the angiogenesis dependent disease is not rheumatoid arthritis.

B 6

18. (Amended) The method of Claim 16 wherein the angiogenesis dependent disease is selected from macular degeneration, diabetic retinopathy, neovascular glaucoma, retrothalental fibroplasia, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phlyctenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft/rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosus, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

Sub DD

19. (Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an antiinflammatory compound, with the proviso that the angiogenesis inhibiting compound is not thalidomide.

21 20. (Amended) The method of Claim 19 wherein the angiogenesis dependent disease is selected from macular degeneration, diabetic retinopathy, neovascular glaucoma, retrothalic fibroplasia, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phlyctenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosus, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

BT 21 21. (Amended) The angiogenesis inhibitory composition of Claim 21 wherein the steroid is selected from cortisol, corticosterone, hydrocortisone, hydrocortisol, cortisone, prednisone, prednisolone, dexamethasone, beclomethasone, betamethasone, mometasone, mometasone furoate, budesonide, triamcinolone acetonide, or fluticasone.

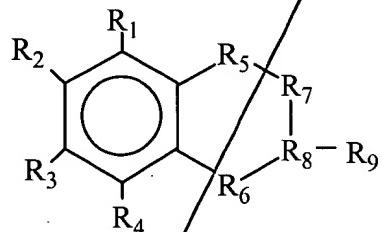
B8 24 24. (Amended) The angiogenesis inhibitory composition of Claim 23 wherein the NSAID is selected from aspirin, acetaminophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguaiaretic acid (NDGA), sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398 (a cyclooxygenase-2 inhibitor), cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecasa, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, floctafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, pirprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, or tenoxicam.

~~14~~ ¹² (Amended) The angiogenesis inhibitory composition of Claim ~~23~~ wherein the NSAID is selected from indomethacin or sulindac.

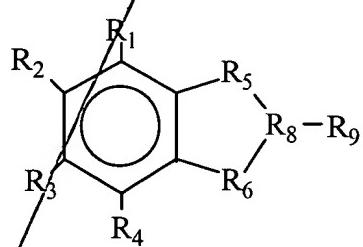
~~23~~ ²³ (Amended) A method for inhibiting angiogenesis in a human or animal comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, wherein the angiogenesis inhibiting compound is selected from:

(1) a compound selected from the formula

A)

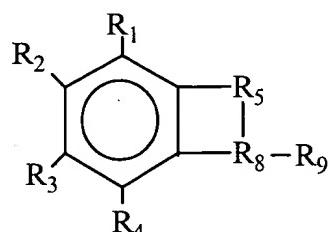


B)



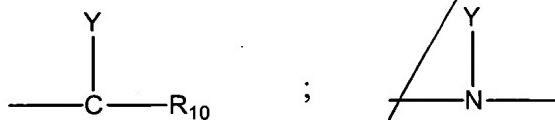
or

C)



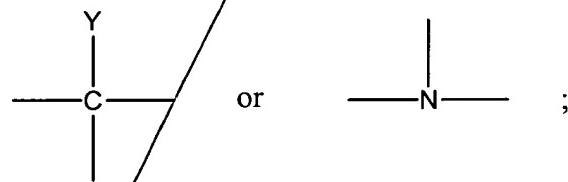
wherein

$R_1 - R_4$ are each independently selected from -H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; $-XO_n$ or $-O-XO_n$, where $X=N$ and $n=2$, $X=S$ and $n=2$ or 3, or $X=P$ and $n=1-3$; and halogens;
 $R_5 - R_7$ are each independently selected from



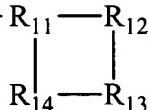
or -O-, where Y is absent and R₁₀ is =O or Y and R₁₀ are each independently the same as R₁;

where R₈ is independently selected from:

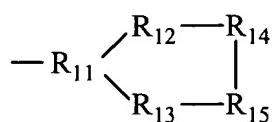


and R₉ is a moiety selected from

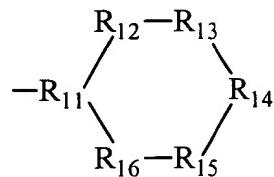
D)



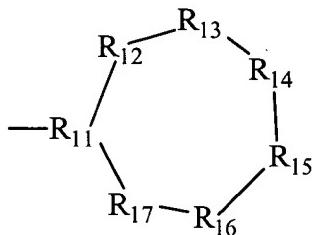
E)



F)

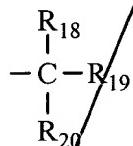


G)



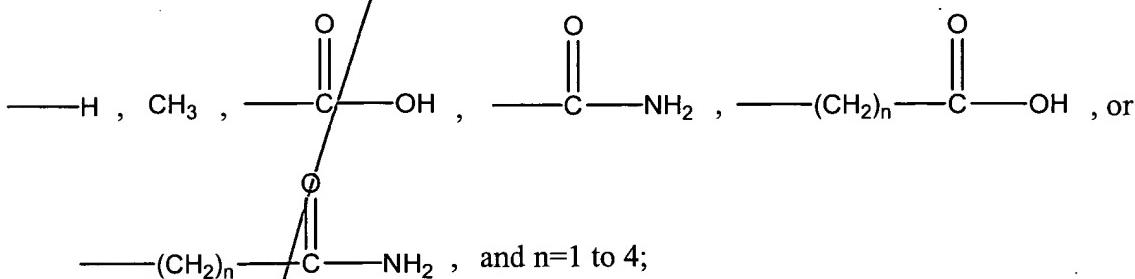
or

H)



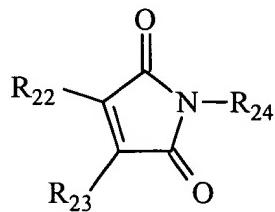
wherein

each of R₁₂-R₁₇ is independently the same as R₅, wherein R₁₁ is independently the same as R₈; and wherein R₁₈, R₁₉ and R₂₀ are each independently selected from



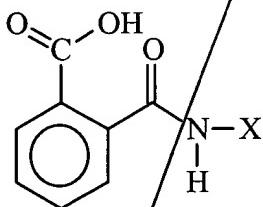
with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound selected from the formula

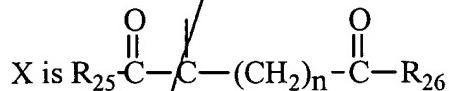


where R₂₂ and R₂₃ are each independently H, F, Cl, Br, I, CH₃, or -CH₂-CH₃;
and R₂₄ is H, CH₃, or -CH₂-CH₃;
and

R 8 (3) a compound selected from the formula



where X is R₆ as defined in (1) above, or



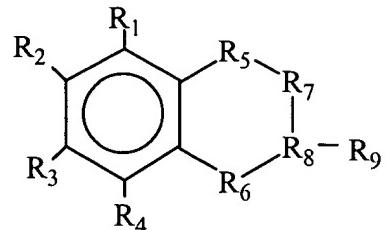
and R₂₅ and R₂₆ are independently -OH, -H, or -NH₂, and n = 1 through 4.

29. 27. (Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an antiinflammatory compound

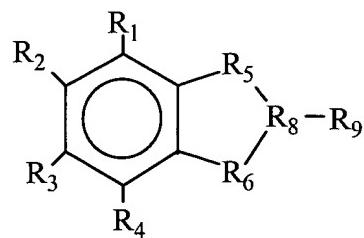
wherein the angiogenesis inhibiting compound is selected from:

(1) a compound selected from the formula

A)

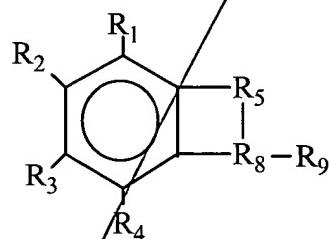


B)



or

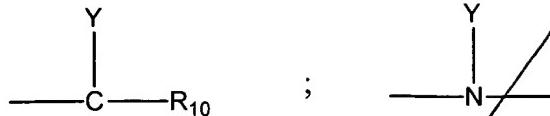
C)



wherein

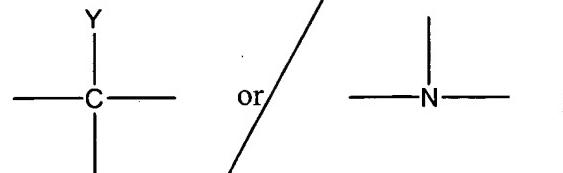
R₁ - R₄ are each independently selected from -H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; -XO_n or -O-XO_n, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens;

$R_5 - R_7$ are each independently selected from



or $-O-$, where Y is absent and R_{10} is $=O$ or Y and R_{10} are each independently the same as R_1 ;

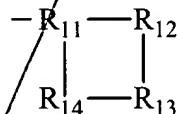
where R_8 is independently selected from:



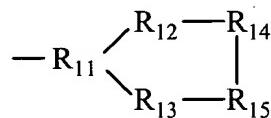
E1
~~B8~~
Cont

and R_9 is a moiety selected from

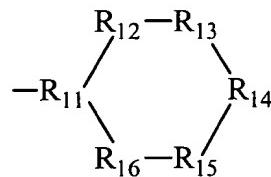
D)



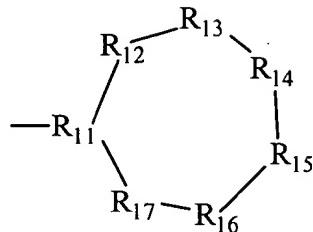
E)



F)

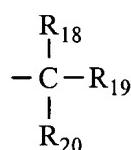


G)



or

H)



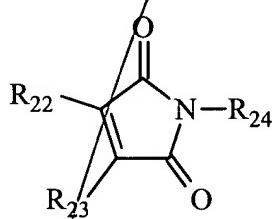
wherein each of R₁₂- R₁₇ is independently the same as R₅, wherein R₁₁ is independently the same as R₈; and wherein R₁₈, R₁₉ and R₂₀ are each independently selected from

BS
cont
—H , CH₃ , —C=O—OH , —C=O—NH₂ , —(CH₂)_n—C=O—OH , or

—(CH₂)_n—C=O—NH₂ , and n=1 to 4;

with the proviso that the angiogenesis inhibiting compound is not thalidomide;

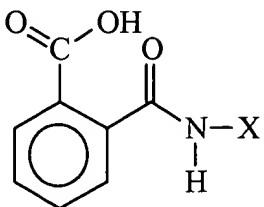
(2) a compound selected from the formula



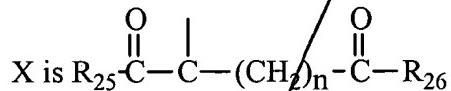
where R₂₂ and R₂₃ are each independently H, F, Cl, Br, I, CH₃, or -CH₂-CH₃;

and R_{24} is H, CH_3 , or $-CH_2-CH_3$;
and

(3) a compound selected from the formula



where X is R_6 as defined in (1) above, or



and R_{25} and R_{26} are independently -OH, -H, or -NH₂, and n = 1 through 4.

³⁰ ~~28~~. (Amended) The method of Claim ²⁹ ~~27~~ wherein the angiogenesis dependent disease is selected from macular degeneration, diabetic retinopathy, neovascular glaucoma, retrobulbar fibroplasias, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phlyctenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosis, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, or rubeosis.

B9 6
44. (Amended) The angiogenesis inhibitory composition of Claim 43 wherein the NSAID is selected from aspirin, acetominophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguaiaretic acid (NDGA), sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398 (a cyclooxygenase-2 inhibitor), cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecasa, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, floctafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, pirprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, or tenoxicam.